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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

re Application of:

Bernd RIEDL et al.		Confirmation No.:	9631
Serial No.:	10/071,248	Examiner:	Rita J. Desai
Filed:	February 11, 2002	Group Art Unit:	1625

Title: METHOD AND/OR PROCESS FOR PREPARING ω-CARBOXYARYL SUBSTITUTED DIPHENYL UREAS AS RAF KINASE INHIBITORS

REPLY BRIEF

Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the Examiner's Answer mailed June 14, 2007, herewith is Appellant's Reply Brief.

The Examiner's Answer does not present any new issues in maintaining the rejection of claims 1-15 and 22 under 35 U.S.C 112, first paragraph, and Appellants submit the arguments presented in the Brief on Appeal are adequate to rebut the reasons given for this rejection in than no objective evidence has been presented that the disclosure within the specification does not enable one skilled in the art to make and use the compounds claimed (claims 1-15) or to perform the treatment methods claimed (claim 22).

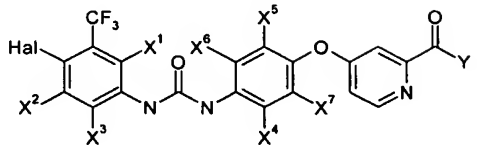
This Reply Brief is presented in response to the following points of argument raised in the Examiner's Answer to support the rejection:

1) On page 3, lines 16-17, of the Examiner's Answer, it is alleged,

> "The invention is to compounds with a specific position hydroxyl or –OC(O)C_1-C_4 alkyl group [SIC]to treat osteoporosis and inflammation."

This interpretation of the invention is too narrow. The invention is directed to

(A) compounds of formula (Ia)



(Ia)

with no restrictions on their use, and

(B) methods of treating osteoporosis and inflammation with a compound of formula Ia.

2) On pages 3 and 4 of the Examiner's Answer, the state of the prior art is said to be that of "drugs."

The compounds of claims 1-15 are not limited to drugs.

3) On page 4 of the Examiner's Answer, the interpretation of the predictability in the art focuses on the treatment of osteoporosis and inflammation.

This interpretation is too narrow with respect to compounds of claims 1-15. Contrary to the allegations made in the Examiner's Answer, the examples do show raf kinase inhibition is retained with significant changes in the structure of similar urea compounds. From these examples, one skilled in the art would not doubt the claimed compounds inhibit raf kinase and from the disclosure one skilled in the art could use the compounds of claim 1-15 to solid tumors and other cancers mediated by raf kinase, as disclosed on pages 2 and 9-14 of the specification.

4) It is alleged on page 4 and 5 of the Examiner's Answer that the inventor "provides very little direction in the instant application."

The examiner provides no comment on what the disclosure within the application teaches and does not identify any deficiency within this disclosure. The examiner notes that there are no examples of the compounds claims 1-15. However, as stated in the MPEP, "compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed." See MPEP § 2164.02.

5) It is alleged on page 5 of the Examiner's Answer that, "Since there are no working examples, the amount of experimentation is very high and burdensome."

No evidence has been presented that the preparation and use of the compounds of claims 1-15 requires undue experimentation. As admitted on page 6 of the Examiner's answer, "The examiner has not raised the issue of how to make the compounds." The Examiner's answer instead questions, "whether the starting materials or apparatus necessary to make the invention are available."

As disclosed in page 19 of the specification, the diaryl ureas of this invention can be derived from substituted anilines. One skilled in the art would recognize that the substituted anilines needed to make the compounds of claims 1-15, if not commercially available, could be prepared by methods known in the art. The specification discloses on page 15, lines 20-23 that substituted anilines needed to prepare compounds of the invention could be prepared by text book chemistry, such as the text book methods disclosed in *Advanced Organic Chemistry*, 3rd Edition, John Wiley, 1985.

In addition, on page 65 of the specification under the heading,

> D5. General Method for the Deprotection of *N*-(ω-Silyloxyalkyl)amides. Synthesis of *N*-(4-Chloro-3-((trifluoromethyl)phenyl)-*N'*-(4-(4-(2-(*N*-(2-hydroxy)ethylcarbamoyl)pyridyloxyphenyl) Urea,

the use and removal of protective groups which results in a hydroxy group on a compound with a similar structure to those of claims 1-15 is disclosed. Based on these disclosures, the specification clearly enables those skilled in the art to make the compounds of claims 1-15.

Evidence that those skilled in the art could obtain suitable substituted aniline starting materials by conventional chemistry without undue experimentation is the disclosure within US Patent 5,886,044. At column 24, lines 5-15, of this patent a synthesis method for preparing hydroxy anilines is disclosed. At column 58, lines 29-30, of this patent the use of the aniline starting material: 4-trifluoromethyl-3-fluoro-2-hydroxy aniline is disclosed. This compound which is very close in structure to anilines suitable for use in preparing the compounds of claims 1-15. One need only replace the fluorine with chlorine.

6) Pages 7-15 of the Examiner's Answer list diseases which are encompassed by the term "inflammation."

While the scope of disease is broad, no evidence has been presented to suggest that the claimed compounds can not treat any of the diseases listed.

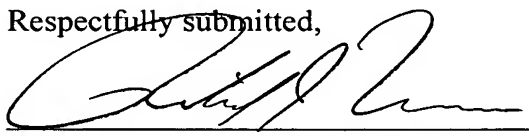
7) Pages 16 and 17 repeat the point that there are no working examples, assays for efficacy or dosage ranges for the treatment method.

These arguments only pertain to claim 22 since there are assays and dosage ranges for raf kinase activity disclosed in the specification, which are relevant to the compounds of claims 1-15.

As to the methods of treatment of claim 22, as discussed in the Appeal Brief, it is well settled that dosage ranges and assays are not required to satisfy the statute, particularly since no evidence has been presented to doubt the disclosure within the application. Any experimental study into suitable dosage ranges and efficacy of the compounds which is necessary would be routinely performed on a day-to-day basis and would not be an undue burden.

For the reasons stated above and in the Brief on Appeal, Appellants respectfully submit the subject matter of the claims on appeal satisfy the requirements of 35 U.S.C. §112, first paragraph. Therefore, Appellants respectfully request the outstanding rejection be reversed.

Respectfully submitted,



Richard J. Traverso, Reg. No. 30,595
Attorney/Agent for Applicants
703 812 5310

MILLEN, WHITE, ZELANO &
BRANIGAN, P.C.
Arlington Courthouse Plaza 1, Suite 1400
2200 Clarendon Boulevard
ARLINGTON, VIRGINIA 22201

Attorney Docket No.: **Bayer -0015-p04**

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